



THE

SISTER STUDY

BREAST CANCER RESEARCH

WOMAN BY WOMAN, SISTER BY SISTER, WE CAN MAKE A DIFFERENCE!

NOVEMBER 2024

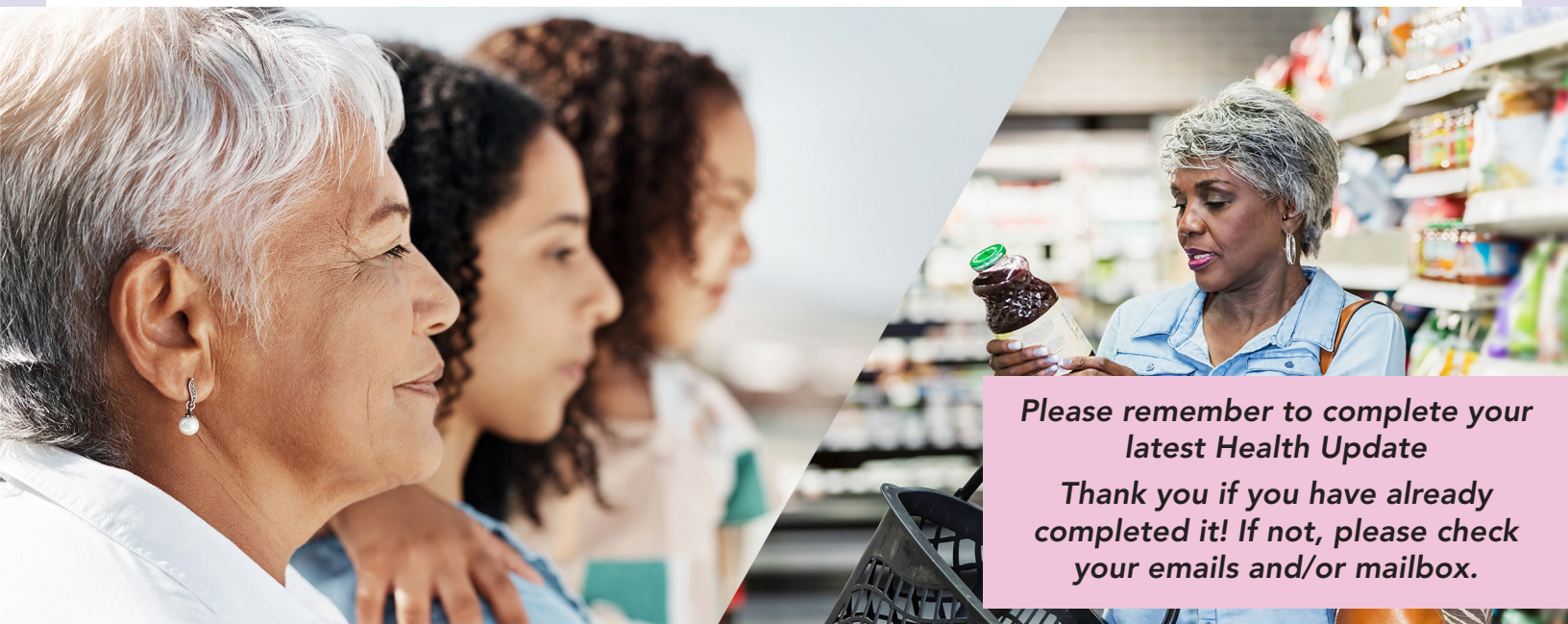
Dear Sisters —

To help you keep up with the latest Sister Study news, we plan to send you periodic flyers with our latest updates. You will also find the latest news on our Sister Study website sisterstudy.niehs.nih.gov/English/new.htm and on our Sister Study Facebook group page. **To join our Facebook group**, search for “NIEHS Sister Study” on Facebook, scroll to the right of the top bar, click “Groups”, and ask to join our private group. You may also follow this direct link www.facebook.com/groups/niehsisterstudy.

Thank you for helping our researchers continue to advance breast cancer research!

Breast Cancer Risk Prediction Considering Genetic and non-Genetic Risk Factors

We know that breast cancer risk can be influenced by both genetic and non-genetic factors, but our understanding of the combined effects of these various factors is limited. The Sister Study recently contributed to a study that used data on (1) rare, pathogenic variants of genes associated with high risk of breast cancer (e.g., BRCA1, BRCA2, and CHEK2), (2) more common genetic mutations, and (3) various epidemiologic factors to predict breast cancer risk. The authors illustrate how epidemiologic risk factors (including reproductive history, lifestyle, and clinical factors) can **help determine who has the highest risk among women who are known to be at increased risk due to their genetic profile**. As an example, having a mutation in the CHEK2 gene was **highly predictive of risk overall** (>20% lifetime risk), but adding information on other genetic and non-genetic factors could further divide CHEK2 carriers into those who would (or would not) most benefit from regular MRI screening. More details on specific combinations of risk factors are provided in the published manuscript. tinyurl.com/BrCaGenRisk



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Thank you if you have already completed it! If not, please check your emails and/or mailbox.

Per- and Polyfluoroalkyl Substances (PFAS) and Breast Cancer Risk

One of the main aims of the Sister Study is to identify environmental risk factors for breast cancer. To achieve this, we learn from and build upon earlier studies of chemicals that are suspected to be harmful but are not established carcinogens. Chemicals of current concern are the so called “forever chemicals”: per- and

polyfluoroalkyl substances (PFAS) that are found in water, air, fish, and soil as well as many different consumer and commercial products. **PFAS have been found in the blood of people all over the world.** In preparation for investigating PFAS in the Sister Study, several investigators reviewed the results of prior studies. Some of these showed that higher blood concentrations of certain PFAS may be associated with **increased future breast cancer risk**, but the authors noted inconsistencies across studies and identified some major limitations. They concluded that the association between PFAS exposure and breast cancer is not yet established and identified some areas where additional or more in-depth research is needed.

tinyurl.com/PFASBrCa

Air pollution and ovarian cancer

Outdoor air pollution has been linked to various cancers, including lung, breast, and uterine cancers, but its association with ovarian cancer, a gynecologic cancer with poor survival, has been less studied. In the Sister Study, we estimated participants' exposure to air pollutants—nitrogen dioxide (NO₂), particulate matter (PM_{2.5}), and ozone (O₃)—based on residential addresses. Our analysis found that higher NO₂ levels, which are often an indication of high traffic pollution, were **linked to an increased risk of ovarian cancer**. The relationship between ovarian cancer and exposure to PM_{2.5} or O₃ was less consistent. These findings suggest that air pollution, particularly NO₂, may play a role in ovarian cancer development. tinyurl.com/AirPollOvCa



Women Fibroids, endometriosis and ovarian cancer

Uterine fibroids and endometriosis are two non-cancerous gynecological conditions that share some symptoms. Both conditions are influenced by hormones such as estrogen and there is some evidence they **may be associated with ovarian cancer risk**. Some women with these conditions have their uterus removed (hysterectomy), which could also impact their ovarian cancer risk. In the Sister Study, 34% of 40,928 eligible participants have reported a fibroid diagnosis, 13% reported having had endometriosis, and 7% reported having both. 20% of participants have had a hysterectomy. **Women with fibroids had a 65% increased rate of developing ovarian cancer, compared to women without fibroids.** Among women with fibroids, those who had a hysterectomy were less likely to develop ovarian cancer than those who did not. History of endometriosis was not associated with risk. Studying the joint effects of fibroids, endometriosis and hysterectomies adds to our understanding of ovarian cancer and may help inform decisions about how women with fibroids, endometriosis, and hysterectomies are treated and monitored. tinyurl.com/FibEndoOvCa

Understanding the genetic complexity of puberty timing across the allele frequency spectrum

The age at which girls go through puberty can vary considerably and has been linked to health outcomes later in life. For example, earlier puberty is associated with an **increased risk of developing breast cancer**. Information collected from Sister Study participants was recently included in a study of the genetic factors associated with age at puberty onset. Study authors identified **more than 1,000 genetic variants potentially linked to pubertal age**. These results are being used to identify some of the key genes and biological pathways that impact puberty and its links to disease later in life. tinyurl.com/PubTimeAllele



A Big Thanks to Our Generous Sister Study Sisters!

Since we began analyzing the data provided by our generous Sisters, **our researchers have published over 300 scientific papers!** These findings contribute to improvements in our understanding of the environmental and genetic causes of breast cancer and other important issues in women's health. We are proud of what we have accomplished together with our study sisters! Thank you for sticking with us!



As always, please contact us at the Sister Study helpdesk toll-free at 877-4SISTER (877-474-7837) or email us at update@sisterstudy.org if you have updates or questions.

To view our study findings, please visit our Sister Study website: tinyurl.com/SISDiscoveries